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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,186	07/20/2001	Leonard A. Smith	A33626A 067252.0107	8442
21003	7590	05/16/2005		EXAMINER
BAKER & BOTTS 30 ROCKEFELLER PLAZA NEW YORK, NY 10112				PORTNER, VIRGINIA ALLEN
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 05/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/910,186	SMITH ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 10 February 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 42,43,45-51,53,55,56,82,85 and 86 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 42-43, 45-51, 53, 55-56, 82,85-86 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

Claims 42-43, 45-51, 53, 55-56, 82,85-86 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 10, 2005 has been entered.

Priority

1. Applicant's claim for priority is acknowledged, in light of the amendment of the first sentence of the Specification to define a specific relationship between Applicant's co-pending Applications.

Claim Objections

2. Claims 48, 53,82 is objected to because of the following informalities:
3. Claim 48 in the "tranfecting" paragraph utilizes a nucleic acid that encodes a polypeptide of SEQ ID NO 8, but the expressed polypeptides has an amino acid sequence other than SEQ ID NO 8, in light of claim 49 defining the sequence to be SEQ ID NO 8; this is confusing. The "culturing" paragraph of claim 48 should recite SEQ ID NO 8. Claim 49 is not further limiting of claim 48 in light of Applicant's amendment to remove the phrase "havng at least one immunogenic epitope".

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4. Claim 53 recites the term "mammalian cell", but the specification defines the host cells to be "mammalian cell lines, see [0020]"; claim 53 should be amended to be consistent with the language used to define the invention provided in the instant Specification.
5. Claim 82 recites the phrase "A recombinant host cell"; the cell should be clarified by amending the claim to recite the term "isolated" to differentiate it from cells that recombine in nature.
6. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 42-43, 45-51, 53, 55-56, 82, 85-86 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification broadly describes as part of the invention isolated polynucleotides encoding the polypeptide comprising "SEQ ID NO 8" (see all claims). The specification also broadly describes their novel "botulinum neurotoxin Hc fragment" specifically by a novel reference polynucleotide sequence of SEQ ID NO:7. The specification broadly describes polynucleotides encoding the polypeptide of SEQ ID NO: 8, to specifically include continuous or discontinuous regions encoding the polypeptide and may also contain additional coding and non

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coding regions associated with expression vector sequences. First, it is evident from the specification that applicant is describing their novel "botulinum neurotoxin Hc fragment" nucleic acid specifically by a novel reference polynucleotide sequence which encodes the polypeptide of (SEQ ID NO:8) and generically by a reference polynucleotide sequence of nucleic acids 10-1332 of (SEQ ID NO:7) and that such language is intended to encompass a plurality of sequences, which include "genes" and those coding or non-coding sequences. From the independent claim 42, are dependent claims encompassing vectors (expression control sequences (instant claim 45), host cells and methods of producing the polypeptide (instant claim 53-56. The claims encompass polynucleotide sequences *comprising* SEQ ID NO:7, nucleotides 10-1332, sequences that have a recited degree of change as compared to a reference nucleic acid sequence comprising SEQ ID NO: 7, nucleotides 10-1332, and *comprising* nucleic acids encoding SEQ ID NO:8. None of these sequences meets the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polynucleotide sequence consisting of SEQ ID NO: 7 which corresponds to the polynucleic acid sequence encoding the *botulinum neurotoxin Hc fragment of serotype B* which has cell receptor binding affinity consisting of SEQ ID NO:8. An isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:8, is also described by way of the written description in view of the art established principle of wobble variants of triplet codons for particular bacterial amino acids as described in basic textbooks. Thus, an isolated polynucleotide sequence consisting of SEQ ID NO: 7, nucleotides 10-1332 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:8 meets the written description provision of 35 USC 112, first paragraph.

Applicants have not described nor disclosed the "operon" which encodes the "synthetic botulinum neurotoxin serotype B" gene. A functional bacterial gene encompasses much more than a protein coding region (see Davis et al., Microbiology, page 267). A bacterial gene is

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conventionally associated with positive and negative controlling elements such as promoters and repressors in a concordantly regulated transcription unit called an operon, without which, no protein is expressed. The specification fails to describe the functional gene *per se* (i.e., operon) and which applicants have intended to be encompassed by the comprising and encoding language of the instant claims as set forth *supra*. In a bacterial genome, the recitation of "comprising" SEQ ID NO: 7 or comprising a nucleic acid encoding SEQ ID NO:8, includes regulatory sequences which are essential to the operation and function of the structural gene in the operon. Moreover, the claims encompass and the specification contemplates other open reading frames which are 3' and 5' to the polynucleotide sequence of SEQ ID NO:7 and similarly encoding the amino acid sequence of SEQ ID NO:8, such 5' and 3' information inclusive of the definition of an operon. These regulatory and other gene sequences of the operon that are not described, are essential to the function of the structural gene within the operon and are therefore essential elements. Such sequences fail to have an adequate written description in the instant specification. The specification does not provide written description support for any flanking nucleic acid sequences which are 5' or 3' of SEQ ID NO:7 or that which encodes SEQ ID NO:8. The specification does not provide any polynucleotide structure for a significant fragment or gene segment of the *synthetic Clostridium botulinum neurotoxin* genome, the polynucleotide sequence of the bacterial operon of which SEQ ID NO 7 is a member or the gene in the operon as conventionally accompanied by the regulatory elements (i.e., regulatory regions such as promoters or repressors, termination codon), and which comprises SEQ ID NO:7. With the exception of an isolated polynucleotide consisting of SEQ ID NO: 7, nucleotides 10-1332 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:2, the skilled artisan cannot envision all the contemplated nucleotide sequences by the detailed chemical structure of the claimed polynucleotides and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required.

See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian

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FGF's were found unpatentable due to lack of written description for the broad class. Similarly, applicants have not disclosed any information which is 3' and 5' to the polynucleotide sequence of SEQ ID NO: 7, nucleotides 10-1332 and therefore clearly lacks written description for the broad class of polynucleotides comprising SEQ ID NO:7, nucleotides 10-1332. Thus, the written description of the instant specification does not provide for "comprising" language. In the instant case the specification provides only written description for a polynucleotide consisting of SEQ ID NO:7, polynucleotides 10-1332 and a polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:8.

Therefore, only an isolated polynucleotide consisting of SEQ ID NO: 7, nucleotides 10-1332 and an isolated polynucleotide consisting of a nucleotide sequence encoding SEQ ID NO:8, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999. Claims directed to an isolated nucleic acid encoding a fusion protein comprising a polynucleotide encoding the amino acid sequence consisting of SEQ ID 8 could possibly obviate this rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VGP
May 12, 2005

LR
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SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600